



PTO/SB/21 (04-04) 1642

**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

Application Number	09/622,613
Filing Date	August 17, 2000
First Named Inventor	Rybak, Susanna M
Art Unit	1642
Examiner Name	Yu, Misook
Attorney Docket Number	015280-343100US

Total Number of Pages in This Submission

ENCLOSURES (Check all that apply)

- | | | |
|--|---|--|
| <input type="checkbox"/> Fee Transmittal Form
<input type="checkbox"/> Fee Attached
<input checked="" type="checkbox"/> Amendment/Reply - "Supplemental Response" w/Appendices A and B
<input type="checkbox"/> After Final
<input type="checkbox"/> Affidavits/declaration(s)
<input type="checkbox"/> Extension of Time Request-
<input type="checkbox"/> Express Abandonment Request
<input type="checkbox"/> Information Disclosure Statement
<input type="checkbox"/> Certified Copy of Priority Document(s)
<input type="checkbox"/> Response to Missing Parts/Incomplete Application
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s)
<input type="checkbox"/> Licensing-related Papers
<input type="checkbox"/> Petition
<input type="checkbox"/> Petition to Convert to a Provisional Application
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<input type="checkbox"/> CD, Number of CD(s) _____ | <input type="checkbox"/> After Allowance Communication to Technology Center (TC)
<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Status Letter
<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
Return Postcard |
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Remarks	The Commissioner is authorized to charge any additional fees to Deposit Account 20-1430.
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SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Townsend and Townsend and Crew LLP
Signature	Jean M. Lockyer, Ph.D.
Date	August 4, 2004
	Reg. No. 44,879

CERTIFICATE OF TRANSMISSION/MAILING

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Malinda C. Dagit

Date

4 Aug. 2004



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On 4 Aug. 2004

TOWNSEND and TOWNSEND and CREW LLP

By: Malinda Dagut

PATENT

Attorney Docket No.: 015280-343100US

Client Ref. No.: E-029-98/1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

RYBAK and NEWTON

Application No.: 09/622,613

Filed: August 17, 2000

For: RECOMBINANT ANTI-TUMOR
RNASE

Customer No.: 20350

Confirmation No. 8380

Examiner: Yu, Misook

Technology Center/Art Unit: 1642

SUPPLEMENTAL RESPONSE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is supplemental to Applicants' response (mailed July 29, 2004) to the Office Action of January 29, 2004.

Enclosed herewith is a Declaration under 37 C.F.R. § 1.132 by Dianne Newton (referred to herein as "the Newton Declaration"). In order to expedite prosecution, Applicants submit the Newton Declaration to provide additional data that shows that the claimed recombinant RNase molecules are active.

The data presented in the Newton Declaration shows that recombinant RNase molecules, *e.g.*, rapLR1, as set forth in the claims having a glutamine at the N-terminus are active in a direct RNase activity (*see*, section 3, Appendix A of the Newton Declaration). The data in Appendix A show the tRNase activity of rapLR1.

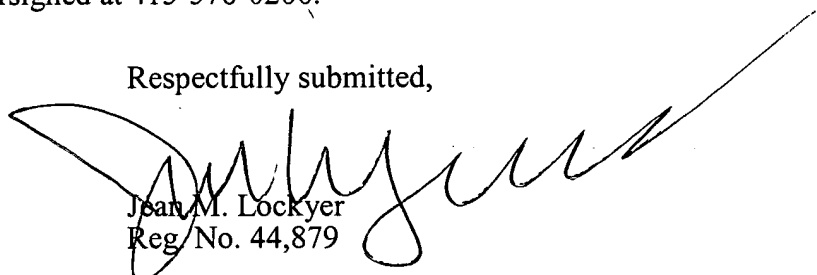
The Declaration also includes the results of a protein sequence determination (section 4, Appendix B) that shows that there is a glutamine present at position 1 of rapLR1. Further, the sequence determination shows that the N-terminus is not a pyroglutamic acid, as the presence of the residue would have blocked it.

In summary, the Newton Declaration provides additional evidence that the claimed RNase molecules that have a glutamine at position 1 are active.

Applicants also note that there was a typographical error on page 14 of the response mailed July 29, 2004. The first sentence of the second full paragraph on that page should read "the art cited on page 4 of the Office Action".

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Jean M. Lockyer
Reg. No. 44,879

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60276942 v1



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PATENT
Attorney Docket No.: 015280-343100US
Client Ref. No.: E-029-98/1

~~Assistant~~ Commissioner for Patents
Washington, D.C. 20231

Alexandria, VA 22313

On

4 Aug. 2004

TOWNSEND and TOWNSEND and CREW LLP

By:

Malwida Dofit

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

RYBAK and NEWTON

Application No.: 09/622,613

Filed: August 17, 2000

For: RECOMBINANT ANTI-TUMOR
RNASE

Examiner: Yu, Misook

Art Unit: 1642

DECLARATION OF DIANNE NEWTON
UNDER 37 C.F.R. §1.132

I, Dianne Newton, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. § 1001, and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. I currently hold a position as a Senior Scientist at SAIC Frederick, the National Cancer Institute of the National Institutes of Health. I am an inventor on the subject application.. I have over 13 years of experience in this field. The data presented here was obtained from experiments performed by me or under my supervision.

2. It is my understanding that in the Office Action mailed January 29, 2004, the Examiner rejects the claims as allegedly not enabled. In particular, the Examiner argues that it would require undue experimentation to practice the claimed invention because:

RYBAK and NEWTON
Application No.: 09/622,613
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PATENT

the art teaches that position 1 of ONCONASE-related ribonucleases is important for activity, and the activity of a ribonuclease that has a different residue at position 1 can only be determined empirically. The Examiner further appears to believe that the specification does not demonstrate that the proteins of the invention that have a glutamine at position 1 also have ribonuclease activity. This Declaration provides further evidence that the claimed sequences have ribonuclease activity.

3. Table II on page 45 of the specification shows the cytotoxicity of recombinant RNases in various cell lines. The results indicate that recombinant rapLR1 is cytotoxic; moreover, in most instances, it exhibits enhanced cytotoxicity relative to recombinant ONCONASE. The recombinant rapLR1 used in this experiment has the sequence shown in SEQ ID NO:2, which has a glutamine at position 1 (the N-terminal position in SEQ ID NO:2). Further, it has ribonuclease activity, as directly assessed in a ribonuclease activity. Attached as Appendix A is exemplary data showing that recombinant rapLR1 having the sequence of SEQ ID NO:2 is active in a direct ribonuclease activity.

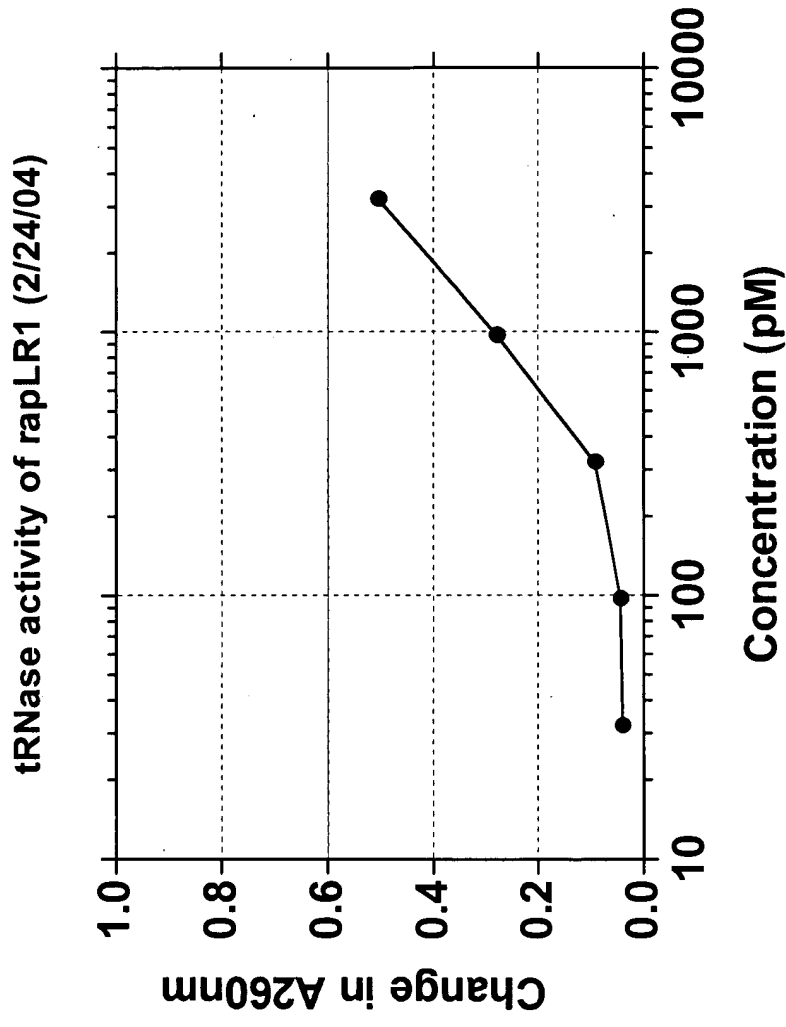
4. To further demonstrate that rapLR1 as set forth in SEQ ID NO:2 has a glutamine at the N-terminus, a sequence analysis was performed on the recombinant protein. Attached as Appendix B is a copy of a page from my laboratory notebook providing the results of the sequence analysis. For lab purposes, rapLR1 was assigned a clone # of 236-11. The sequence analysis shows that a glutamine is present at the N-terminus and the N-terminus is not blocked. A pyroglutamic acid at the N-terminus would block it.

Dated: 8/3/04

By Dianne L. Newton
Dianne L. Newton

Attachments: Exhibit A,B

Recombinant rapLR1 with a glutamine at the NH₂-terminus has ribonuclease activity



Concentration required to cause a change of 0.2nm

—●— rapLR1 std

650 pM

Project No. _____

Book No. _____

81

E End Group Determination RapL1

Page No. _____

10% Tris/Glycine gel - Western transfer

08/31/99 TUE 18:44 FAX 301 846 7119

AIDS VACCINE PROGRAM

1 Std

2 Std

3 "

4 "

5 236

6

7

8

"Cyclized" RapL1

SEQUENCING RESULTS REPORT for SEQ. C-321-B

SAMPLE I.D.

236-11

Requested by

Dr. Newton
SAIC

Charge Acct#

Person Authorised;

Tel;

Fax;

Sequencer; 494 CLC/140C/785A/610A

Run Date

August 27, 1999

Sequence results;

1	2	3	4	5	6	7	8	9	10
Q	D	(W)	L	T					

BEST AVAILABLE COPY

Remarks:

It is not N-terminally blocked.

To Page No. _____

Witnessed & Understood by me,

Date

Invented by

Date

Recorded by